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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/932,483	08/17/2001	Katalin Veronika Lukacs	12071-010002	5360

7590 10/27/2004

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/932,483	LUKACS ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *10 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-31,33,39,40 and 53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11-31,33,39,40 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments and remarks, filed 8/10/04, are acknowledged. In view of said amendments and remarks, all previous rejections under 35 U.S.C. 102 and 103 have been withdrawn. In particular, the recitation of the new limitation of administering a formulation consisting of a heat shock protein has overcome the previous rejections.

2. Claims 1-9, 11-31, 33, 39-40, and 53 are being acted upon.

3. The following are new grounds for rejection.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-9, 11-31, 33, 39-40, and 53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the recitation of "A method to protect a mammal from a disease ...consisting of administering a formulation ... to a mammal having said disease," (Claims 1, 39-40, and 53) is vague and indefinite as it is unclear how a mammal can be protected from a disease it already has.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-9, 11-31, 33, 39-40, and 53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the

claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

Regarding novel methods involving biological processes, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)". The MPEP further states that physiological activity can be considered inherently unpredictable.

A review of the art shows that little is known about the use of heat shock proteins for the treatment of eosinophilic inflammatory responses. There are some teachings that the administration of certain mycobacteria can be used to treat allergic responses, but the active component of the mycobacteria is not known. Accordingly, the specification must be looked to for guidance in the instant case. A review of the specification discloses that the method of the instant claims presumably treats Th2 mediated diseases by administering a heat shock protein to skew the immune response towards Th1. This method is, again presumably, based on the theory that there exists a Th1/Th2 balance wherein increasing the Th1 or Th2 response decreases the other. The experiments disclosed in the specification show that *M. leprae* HSP-65 can induce a T cell response and that administration of *M. leprae* HSP-65 before induction of airway hyperresponsiveness, in a mouse model, can abolish said hyperresponsiveness. Curiously, it is noted that whereas source and grade of other reagents such as ovalbumin is disclosed, the one reagent absolutely critical to the claimed method, the HSP, is merely disclosed as *M. leprae* HSP-65 in PBS, provided by Inventor Lukacs.

First note that many investigators consider the Th1/Th2 paradigm an overly simplistic way to view highly complex systems. See for example Louzoun et al. (2001) wherein the authors attempt to develop a mathematical model to account for contradictory results often seen in attempts to skew the Th1/Th2 ratio, e.g., enhancement (rather than the predicted suppression) of a Th1 mediated disease by the induction of a Th2 response. The authors conclude that Th1 and Th2 cells are more likely markers than effectors in certain diseases. Other authors have concluded that attempts to skew the Th1/Th2 ratio might be dangerous, see for example Brunet et al. (2002).

Even assuming the truth of the Th1/Th2 paradigm, the minimal disclosure of the specification is insufficient given the breadth of the claims. Note that many of the diseases specifically recited in the claims cannot be considered to be strictly Th2 mediated. See, for example, Shimada et al., which teaches that both Th1 and Th2 cytokines play a role in the development of atopic dermatitis. Clearly, simply increasing the Th1 response would not likely provide an effective treatment for this condition. Nance et al. teaches that the interstitial lung disease hypersensitivity pneumonitis is Th1 mediated. Again, increasing the Th1 response would not likely provide an effective treatment for this condition. Also see Mandic et al. which teaches that intrinsic asthma is also called nonallergic asthma (as opposed to extrinsic, allergic, asthma); it is unlikely that increasing the Th1 response would provide an effective treatment for this nonallergic (and non Th2 mediated) condition either.

Also note that not all heat shock proteins comprise the same immunological activities. Even the Inventor's own work, Rha et al. (2002), teaches that of 5 HSPs tested, only an unidentified *M. leprae* HSP had any immunological activity. It must also be noted that many investigators have found that the administration of HSPs can actually *induce* a Th2 response, see for example Francis et al. (2000).

Clearly then, the limited disclosure of the instant specification is insufficient support for the methods of the instant claims. In view of the quantity of experimentation necessary, the lack of sufficient working examples, the unpredictability of physiological activity, and the lack of sufficient specific guidance in the specification, it would take undue trials and errors to practice the claimed invention.

8. Claims 1-9, 11-31, 33, 39-40, and 53 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not

contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, the recitation of, "at least one pharmaceutically acceptable excipient," (Claims 1, 39-40, and 53) is not supported by the specification. The specification teaches only the use of a single pharmaceutically acceptable excipient, not multiple excipients.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973.

11. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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10/21/04
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